

**REMARKS**

**I. Petition for Extension of Time**

Applicants herewith petition the Commissioner for Patents to extend the time for response to the Office Action mailed 2 November 2009 for three (3) months from 2 February 2010 to 2 May 2010. Authorization is given to charge the extension of time fee of \$1110.00 (37 C.F.R. §1.136 and §1.17) to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

**II. Disposition of claims**

Claims 1-10, 12-18 and 21 are pending. Claim 6, 7 and 14 are withdrawn from consideration. Claims 1-5, 8-10, 12, 13, 15-18 and 21 are under examination.

**III. Claim amendments**

Independent claims 1, 5 and 16 have been amended to clarify that the viscosity of the aqueous suspension/ dispersion is 0.05 Pa s or greater, as determined at a shear rate of  $10\text{ s}^{-1}$  from a flow-curve recorded on a rheometer equipped with a plate-plate geometry. Support is provided by the specification at page 16, lines 4-8. Claim 8 has been amended in view of amended claims 1 and 5.

No new matter has been introduced by the claim amendments.

**IV. Claim rejections – 35 U.S.C. §112**

Claim 2 is rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claim 2 has been amended by deletion of the expression modified cellulose derivatives. Withdrawal of the §112 rejection is requested.

**V. Claim rejections – 35 U.S.C. §103**

a. White + Bergstrand + Morris

Claims 1-5, 8-10, 12, 13, 15-18 and 21 are rejected under 35 U.S.C. §103(a) as being unpatentable over White et al., “Delivery of Esomeprazole Magnesium Enteric-Coated Pellets

Through Small Caliber and Standard Nasogastric Tubes and Gastrostomy Tubes *in Vivo*"; Am. J. Health-Syst. Pharm., vol. 59, Nov. 1, 2002, p. 2085-2088 ("White") in combination with US 5,817,338 to Bergstrand et al. ("Bergstrand") and US 5,869,118 to Morris et al. ("Morris").

All claims under examination are expressly characterized by the administration of an aqueous suspension comprising a multiple of enteric coating layered pellets via a gastric tube to a pediatric population. Surprisingly, Applicants have found that the higher the viscosity of the aqueous suspension of the claimed invention the thinner the gastric tubes can be used within certain limits (p. 5, lines 8-12).

The primary reference to White is directed to the delivery of esomeprazole magnesium enteric-coated pellets through nasogastric and gastrostomy tubes *in vivo*. On page 5 of the Office Action, the Examiner acknowledges that White is silent about the inclusion of a thickener in the composition and administration to a pediatric population. In fact, White states in the paragraph bridging pages 2087-2088:

Efficient transit of esomeprazole pellets through feeding tubes may be due to the smaller size and weight of the esomeprazole pellets relative to omeprazole and lansoprazole, the manufacturing process and composition of the enteric coating of the esomeprazole pellets, or both".

The cited paragraph from White suggests that passage of enteric-coated pellets of omeprazole is a factor of (a) the size and weight of the esomeprazole pellets and/or (b) the manufacturing process and composition of the enteric coating. The cited paragraph is conclusive proof of White's failure to appreciate that efficient transit of a enteric coating layered pellets of a proton pump inhibitor through thin gastric tubes, e.g., from CH 5 to CH 10, is possible with a high viscosity suspension/dispersion comprising a thickener as claimed.

Bergstrand discloses an omeprazole formulation that may be dispersed in an aqueous liquid for feeding through a naso-gastric tube and can be administered to a pediatric population. However, Bergstrand is also silent with regard to the use of a thickener or viscous medium to facilitate the administration through narrow gastric tubes suitable for a pediatric population. Specifically, the secondary reference to Bergstrand represents the known disadvantages of the

prior art at the time the claimed invention was made. Although having advantages, administration of enteric coated pellets through a gastric tube as disclosed by Bergstrand - **without a thickener** - has its own disadvantages as disclosed in the specification at page 3, lines 18-25:

- Problems that might arise with administration of enteric coated pellets through gastric tube are for instance caused by the size of the enteric coating layered pellets and the inner diameter the tube or the outlet of the syringe, which might cause clogging in the syringe or tube. This is especially critical for pediatric patients where thin tubes are often required.
- There is also a risk of reduced patient compliance and non-complete dose delivery because of pellets sediment in the glass and/or clogging the syringe used when preparing the suspension. This is especially critical in pediatric use when working with small volumes and doses.

In view of the failure of White and Bergstrand, whether taken alone or in combination, to suggest the claimed invention, the Examiner relies on Morris for the alleged disclosure of gellum gum as the gelling agent in liquid nutritional products to reduce sedimentation and creaming. On the top of page 6 of the Office Action, the Examiner states that “[Morris] discloses composition (sic) with gellum gum as a thickener with a viscosity of less than 0.05 Pa s”. At column 2, lines 21-29, Morris offers the following definitions of high and low viscosity:

*High viscosity products (those over 0.05 Pa s or 50 cps) under high levels of shear stress, are not useful for tube feeding or through a nipple.* As used herein and in the claims, the term “*low viscosity*” means a liquid nutritional product with a viscosity of less than 0.05 Pa s (50 cps) as measured by a Brookfield Viscometer using a #1 spindle at room temperature and at 60 rpm.  
(Emphasis added)

It is an express purpose of the claimed invention to use a high viscosity aqueous suspension/dispersion as the medium to administer enteric coated pellets of an acid labile proton pump inhibitor via a gastric tube to a pediatric population. Disclosing that high viscosity products under high levels of shear stress are not useful for tube feeding, Morris teaches against

the claimed invention. Morris's disclosure of the use of gellan gum to prepare low viscosity nutritional drinks characterized by reduced sedimentation teaches against the claimed method using a high viscosity aqueous medium to transport enteric coated pellets through narrow gastric tubes. Indeed, it is an unexpected advantage in view of Morris that thinner gastric tubes can be used when the viscosity of the aqueous suspension of the claimed invention is 0.05 Pa s or greater. As such, there would have been no motivation at the time the claimed invention was made to combine Morris with White and Bergstrand to arrive at the claimed invention.

For all of the foregoing reasons, a *prima facie* case of obviousness has not been established. Withdrawal of the §103 rejection based on the combination of White, Bergstrand and Morris is requested.

b. White + Bergstrand + Morris + Calanchi

Claims 1-5, 8-10, 12, 13, 15-18 and 21 are rejected under 35 U.S.C. §103(a) as being unpatentable over White, Bergstrand and Morris and further in view of US 6,261,602 to Calanchi et al. ("Calanchi").

Applicants submit that the cited combination of White + Bergstrand + Morris + Calanchi fails for the same reason that the combination of White + Bergstrand + Morris fails to establish a *prima facie* case of obviousness. Specifically, Morris teaches against the use of a high viscosity aqueous suspension/dispersion as the medium to administer enteric coated pellets via a gastric tube to a pediatric population as claimed. In fact, Morris teaches that high viscosity products (those over 0.05 Pa s or 50 cps) under high levels of shear stress are not useful for tube feeding.

Furthermore, Applicants maintain that Calanchi also teaches away from the claimed invention. Calanchi discloses a sachet dosage form prepared from a base granular product made by subjecting one or more thickening agents and one or more disintegrating agents to wet or dry granulation (See claim 1). The granular product is used as a pharmaceutical carrier of pharmaceutical compositions that are capable of rapid suspension in water or aqueous media including saliva. The compositions may be used by addition to a glass of water with stirring or taken directly in the mouth (See Abstract; col. 6, lines 1-8).

In stark contrast to Calanchi, the express purpose of the claimed invention is to provide a solution to the clinical problems associated with the oral administration of enteric coated pellets of a PPI to pediatric patients who are suffering from a gastrointestinal disorder and who may also have difficulties swallowing. For this pediatric population, administration of tablets, capsules or pellets mixed with soft foods or juices is not an option (See p. 2, line 26 to p. 3, line 16).

Thus, the administration routes disclosed by Calanchi - the pharmaceutical composition is poured directly into a glass of water for drinking or poured directly in the mouth for swallowing - are inapposite to the administration route of the claimed invention through a gastric tube. As such, there would have been no motivation at the time the claimed invention was made to consider Calanchi in the development of a method for administering a composition comprising a thickener and a PPI in the form of enteric coating layered pellets via a gastric tube to a pediatric population who may have difficulties swallowing.

For all of the foregoing reasons, a *prima facie* case of obviousness has not been established. Withdrawal of the §103 rejection based on the combination of White, Bergstrand and Morris is requested.

### CONCLUSION

Applicants have made a good faith attempt to respond to the Office Action. For all of the foregoing reasons, claims 1-5, 8-10, 12, 13, 15-18 and 21 are in condition for allowance, which action is earnestly solicited. In view of the allowability of the elected claims, withdrawal of the election of species requirement as to claims 6, 7 and 14 is also requested.

Any fees due in connection with this response should be charged to Deposit Account No. 23-1703.

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Respectfully submitted,

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